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**Single-cell genomics identifies cell type-specific molecular changes in autism.**

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**Public Summary:**

Despite the clinical and genetic heterogeneity of autism, bulk gene expression studies show that changes in the neocortex of autism patients converge on common genes and pathways. However, direct assessment of specific cell types in the brain affected by autism has not been feasible until recently. We used single-nucleus RNA sequencing of cortical tissue from patients with autism to identify autism-associated transcriptomic changes in specific cell types. We found that synaptic signaling of upper-layer excitatory neurons and the molecular state of microglia are preferentially affected in autism. Moreover, our results show that dysregulation of specific groups of genes in cortico-cortical projection neurons correlates with clinical severity of autism. These findings suggest that molecular changes in upper-layer cortical circuits are linked to behavioral manifestations of autism.

**Scientific Abstract:**

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